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جامعة  
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# CNS Stimulants

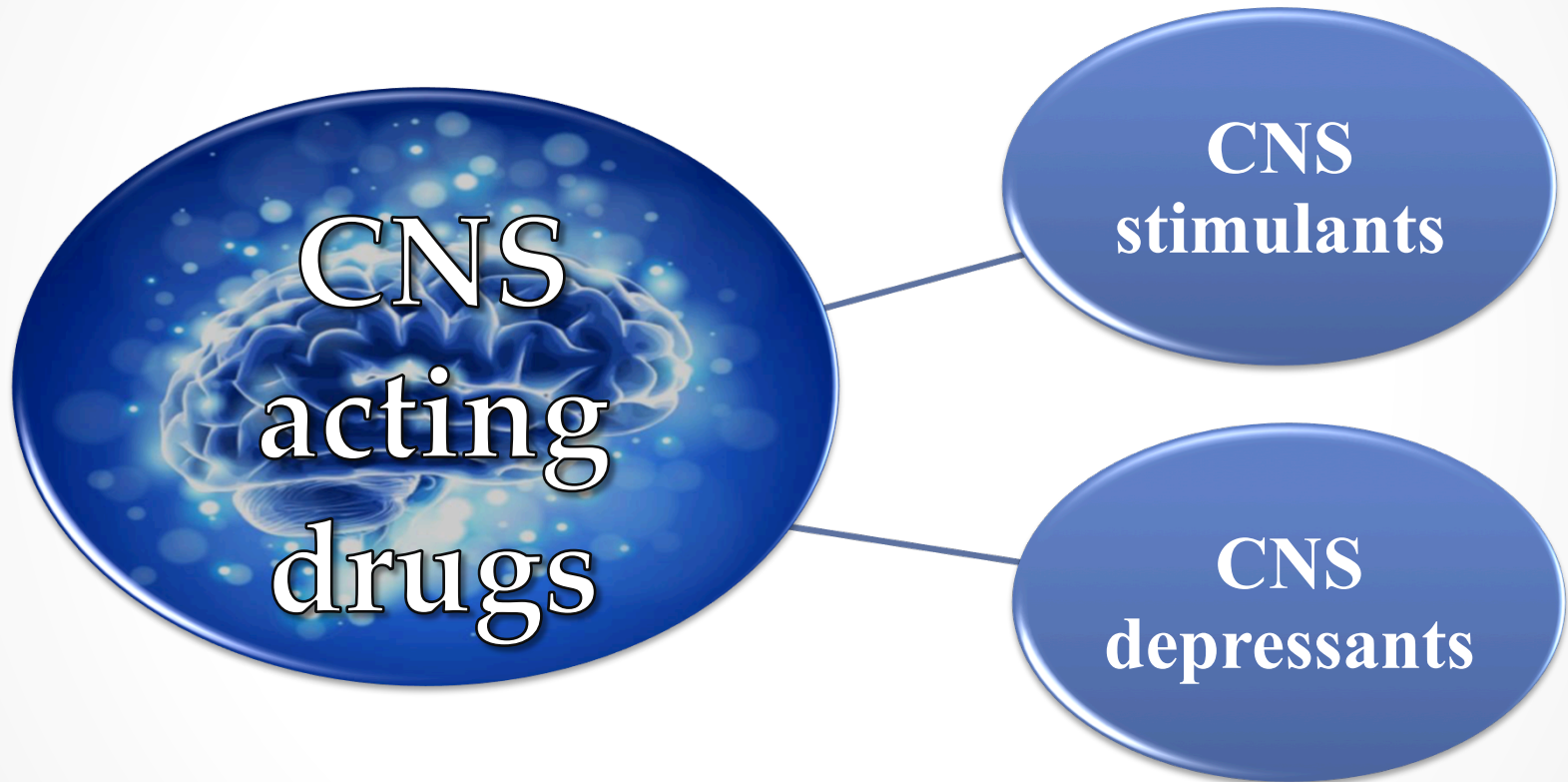
# Objectives

- Discuss the general signs of CNS stimulation.
- Classify the CNS stimulants and illustrate some examples.
- Explain the difference between tonic and clonic convulsions.

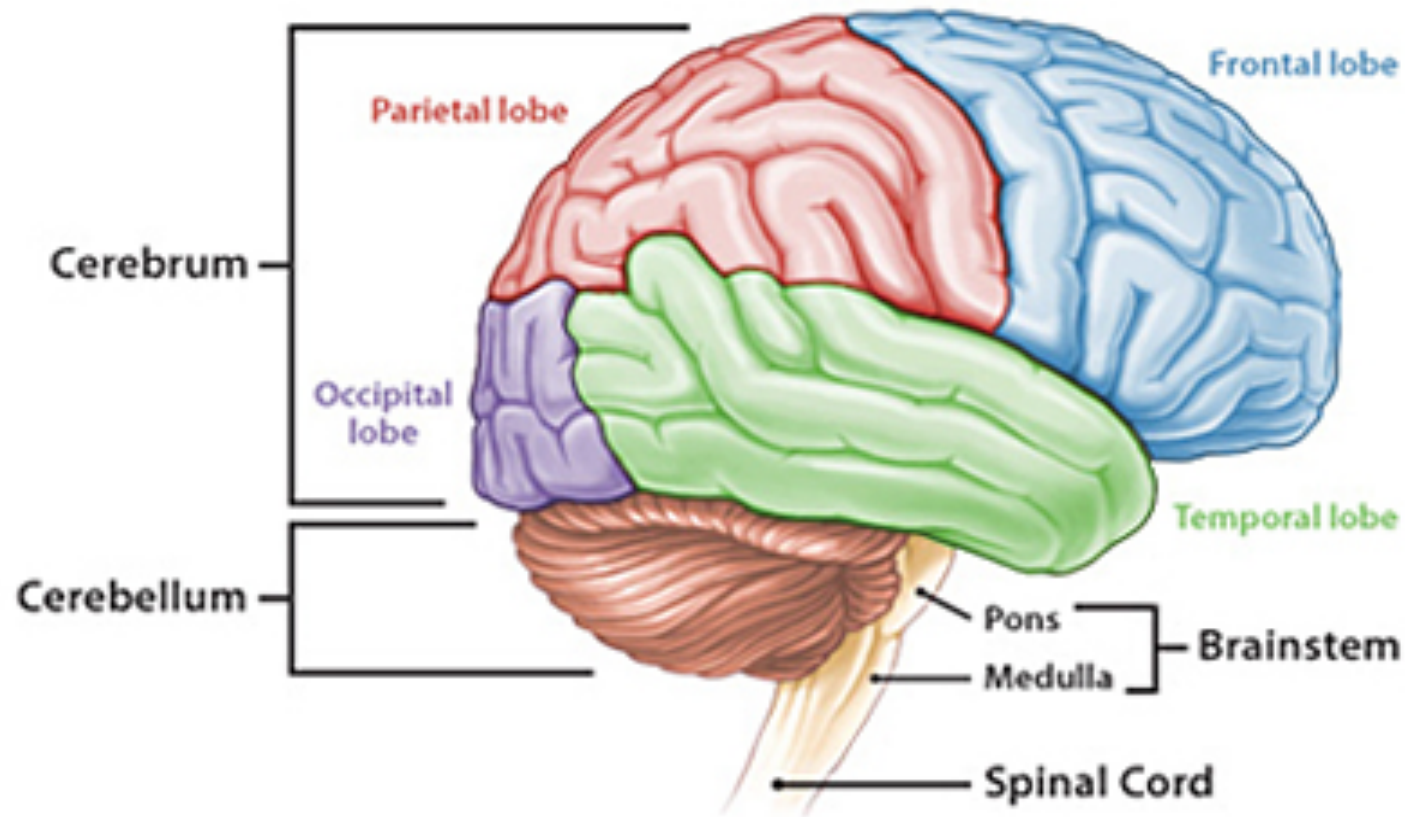
# Pharmacological experiments:

<i>In vitro</i>	<i>In vivo</i>
Using an isolated tissue.	Using a whole animal or intact animal.
Determination of the exact mechanism of action of drug.	Observation of the clinical effect of drug.

# Classification of drugs acting on CNS



# Anatomical features of CNS:



# Anatomical features of CNS:

1. Cerebellum +Pons → equilibrium and coordination of movement.
2. Medulla oblongata → contains the vital center, e.g. respiratory and cardiovascular centers.
3. Spinal cord → responsible for all reflexes.

# CNS stimulants

- They are drugs which increase the muscular (motor) and the mental (sensory) activities.
- Their effects vary from the increase in the alertness and wakefulness (as with caffeine) to the production of convulsion ( as with strychnine) and sometimes lead to death in over dose.

# Classification of CNS stimulants

1. Cerebral stimulants.
2. Psychomotor stimulants e.g. Amphetamine.
3. Medullary stimulants.
4. Psychotomimetic stimulants (hallucinogenic drugs).  
e.g. cannabis, lysergic acid diethylamine (LSD), THC  
(tetrahydrocannabinol).
5. Spinal cord stimulants.



# General signs and symptoms of CNS stimulation:

- ↑ Heart rate.
- ↑ Respiratory rate.
- Instability & restlessness.
- Muscle twitching (tremors).
- Hair erection.
- Convulsion but at high dose may lead to death.

# **Classification of CNS stimulants according to their site of action:**

- Cerebral stimulants.
- Medullary stimulants.
- Spinal cord stimulants.

# Cerebral Stimulants:

<b>Examples</b>	Caffeine and Cocaine
<b>Site of action</b>	Cerebral cortex
<b>MOA</b>	<ol style="list-style-type: none"><li>1. It inhibits phosphodiesterase → ↑ cAMP:<ul style="list-style-type: none"><li>• Stimulates CNS and heart → excitation.</li><li>• Relaxes smooth muscles.</li></ul></li><li>2. A<sub>2</sub> receptors antagonist → CNS stimulation &amp; smooth muscles relaxation.</li></ol>
<b>End point</b>	<ol style="list-style-type: none"><li>1. Hair erection.</li><li>2. Tail erection (onset of action).</li></ol>
<b>High dose</b>	Epileptiform convulsion.
<b>Removed by</b>	Decapitation and pithing.

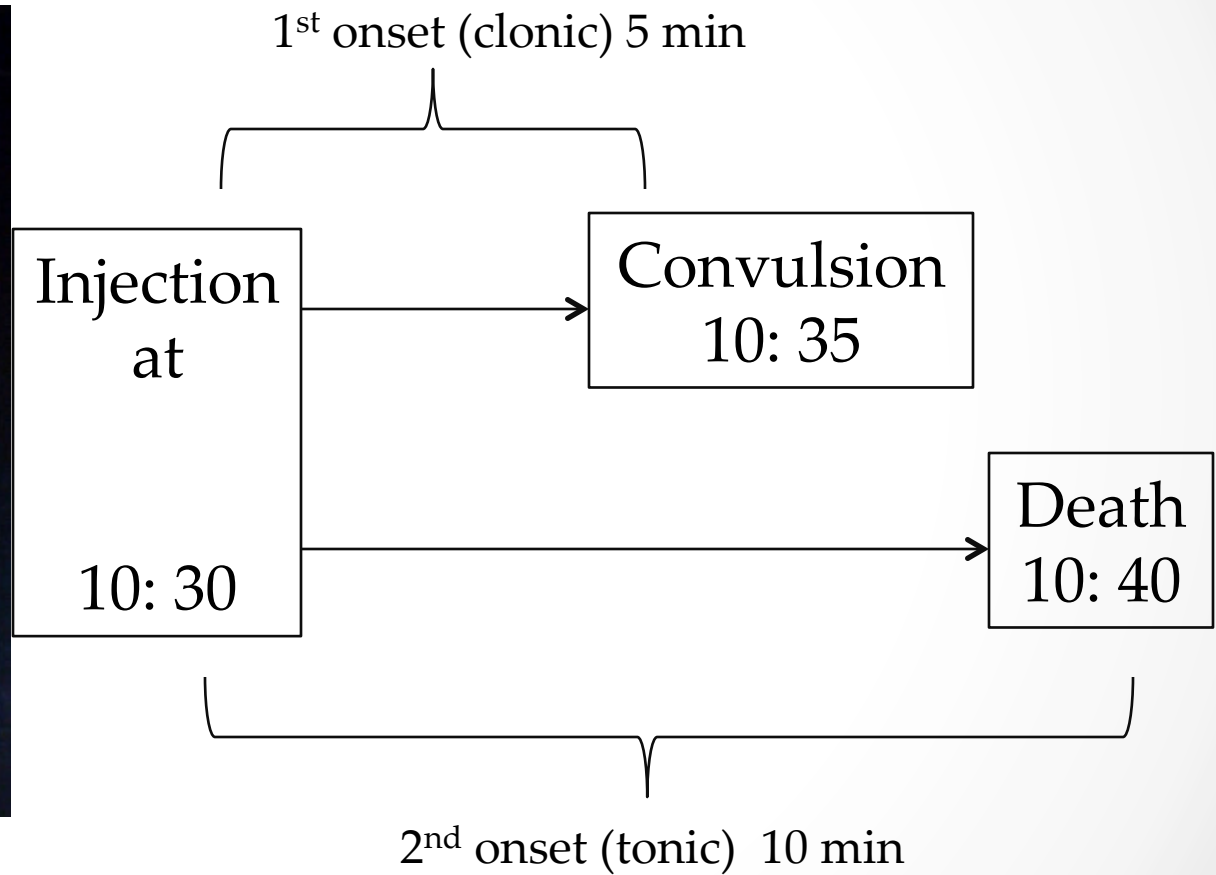
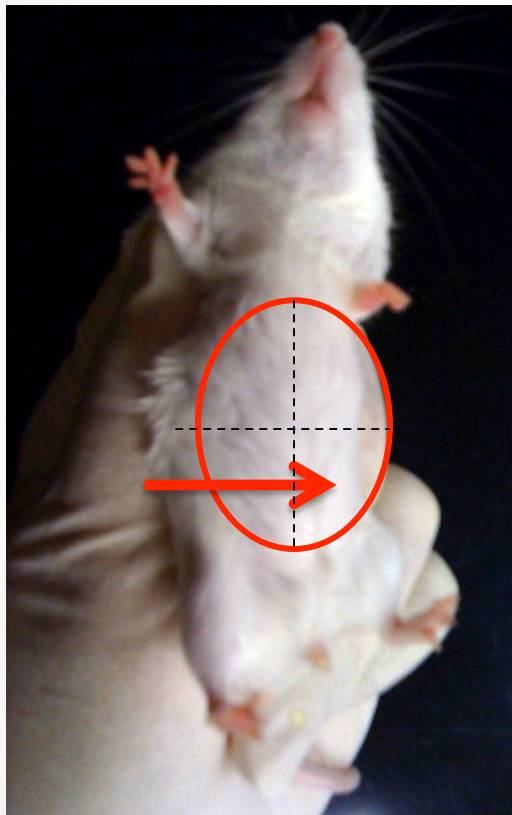
# Medullary Stimulants

Examples	Picrotoxin, Cardiazol, Coramine.
Site of action	Medulla oblongata.
MOA	<ol style="list-style-type: none"><li>1. It inhibits the presynaptic inhibition → decrease GABA.</li><li>2. Noncompetitive GABA<sub>A</sub> receptors blocker which is a chloride dependent → no hyperpolarization → excitation.</li></ol>
End point	Clonic convulsion.
Removed by	Decapitation.

# Characteristics of clonic convulsion:

1. Asymmetric.
2. Coordinated.
3. Intermittent.
4. Spontaneous in origin.
5. It starts as clonic then converted into tonic-clonic & finally to tonic.
6. Removed by decapitation.

# Picrotoxin has 2 onsets of action



# Spinal Cord Stimulant

Example	Strychnine.
Site of action	Spinal cord.
MOA	Block the postsynaptic inhibitory response to glycine by blocking glycine receptors. Glycine is the main inhibitory transmitter acting on motor neurons.
End point	Tonic convulsion.
Removed by	Pithing.

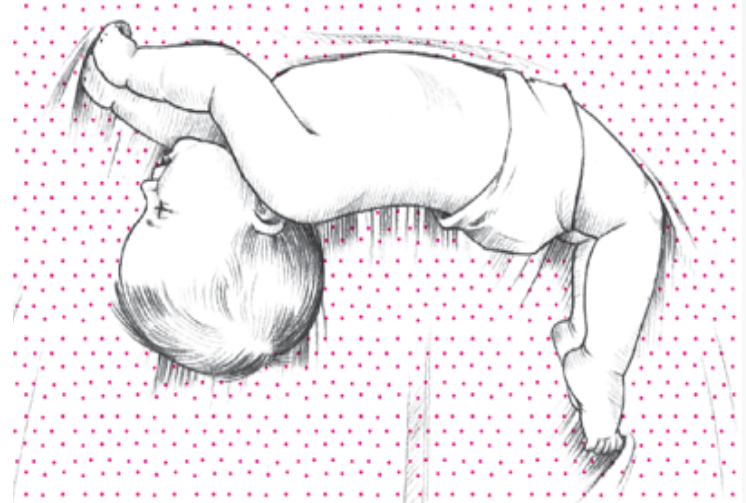
# Characteristics of tonic convulsion:

- Symmetric.
- Non-coordinated.
- Continuous.
- Reflex in origin.
- Characteristic arched back (Opisthotonos posture).
- Removed by pithing.



# Differences between clonic & tonic convulsions:

<b>Clonic</b>	<b>Tonic</b>
<ul style="list-style-type: none"><li>■ Produced by ↑ dose of Medullary stimulants.</li><li>■ Asymmetric (the left side of the body convulsed the right side relaxed).</li><li>■ Coordinated (when the flexors contract the extensors relaxed).</li><li>■ Spontaneous in origin (convulsion develops by its own).</li><li>■ Intermittent.</li><li>■● Removed by decapitation.</li></ul>	<ul style="list-style-type: none"><li>■ Produced by ↑ dose of spinal cord stimulants.</li><li>■ Symmetric (both sides convulsed at the same time).</li><li>■ Non-coordinated (both flexors and extensors contract).</li><li>■ Reflex in origin (need for external stimuli).</li><li>■ Continuous.</li><li>■ Removed by pithing.</li></ul>



# Opisthotonos posture

# Lab work

<b>Drug</b>	<b>Conc.</b>	<b>Dose</b>	<b>Animal</b>	<b>Route</b>
<b>Caffeine</b>	1%	100 mg/kg	Mouse	Intraperitoneal (IP)
<b>Strychnine</b>	0.1%	5 mg/kg		
<b>Picrotoxin</b>	0.5%	25 mg/kg		

# References

- H.P. Rang, M.M. Dale, M.J Ritter, R.J. Flower (2007). CNS stimulants and psychotomimetic drugs. Rang and Dale's Pharmacology, 6<sup>th</sup> edition, Elsevier health sciences, London.